DCTN1 gene

dynactin subunit 1

Normal Function

The *DCTN1* gene provides instructions for making a protein called dynactin-1. At least two different versions of this protein are produced in cells. The two versions differ in size; the larger version is called p150-glued, and the smaller version is called p135.

Both versions of the dynactin-1 protein interact with several other proteins to form a group (a complex) of proteins called dynactin. The p150-glued version of dynactin-1 is the largest component (subunit) of the dynactin complex. This complex plays a critical role in cell division and the transport of materials within cells. To carry out these roles, the complex's p150-glued subunit attaches (binds) to a protein called dynein, which acts as a motor, and also binds to a track-like system of small tubes called microtubules. The dynactin complex, dynein, and microtubules work together like a conveyer belt to move materials within cells.

Researchers believe that the dynactin complex is particularly important for the proper function of axons, which are specialized extensions of nerve cells (neurons). Axons transmit impulses from nerve to nerve and from nerves to muscles. Axons can be quite long; some are more than 3 feet in length. The dynactin complex is a critical part of a rapid transport system that supplies axons with materials to keep them healthy and functioning efficiently.

Health Conditions Related to Genetic Changes

amyotrophic lateral sclerosis

Perry syndrome

At least five mutations in the *DCTN1* gene have been found to cause Perry syndrome. This progressive brain disease is characterized by a pattern of movement abnormalities known as parkinsonism, psychiatric changes, weight loss, and abnormally slow breathing (hypoventilation).

Most of the mutations that cause Perry syndrome change single protein building blocks (amino acids) in the dynactin-1 protein. These genetic changes impair the ability of the p150-glued version of dynactin-1 to bind to the dynactin complex and to microtubules. An incomplete dynactin complex has a reduced ability to transport materials within cells. Slow or abnormal transport of materials needed for the normal function of neurons causes these cells to malfunction and ultimately die. A gradual

loss of neurons in areas of the brain that regulate movement, emotion, and breathing underlies the signs and symptoms of Perry syndrome.

other disorders

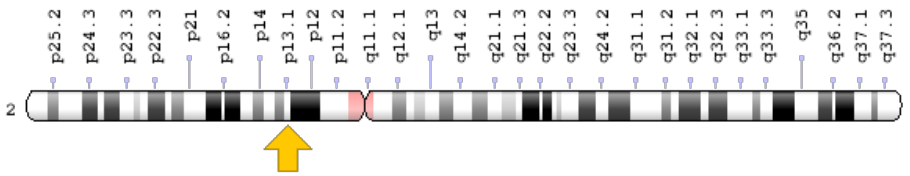
Researchers have identified at least one *DCTN1* gene mutation that causes a nervous system disorder called distal hereditary motor neuronopathy type VIIB. Signs and symptoms of this disorder first appear in early adulthood and include breathing difficulties and progressive weakness of muscles in the face and hands. Muscle weakness in the feet and legs develops later. The mutation that causes this disorder changes one of the amino acids used to make dynactin-1. Specifically, it replaces the amino acid glycine with the amino acid serine at protein position 59 (written as Gly59Ser or G59S). It is unclear how this mutation causes distal hereditary motor neuronopathy type VIIB. The altered protein may result in an abnormal dynactin complex and disturb interactions between the complex and microtubules, which would disrupt transport activities and impair the function of axons in neurons.

At least one *DCTN1* gene mutation is associated with a brain disorder called frontotemporal dementia (FTD) without the features of amyotrophic lateral sclerosis (ALS). This disorder occurs in mid- to late adulthood and is characterized by changes in personality and behavior that may make it difficult for affected individuals to interact with others in a socially appropriate manner. Changes in speech and language can also occur, such as problems using the correct word and difficulty with language comprehension. The *DCTN1* gene mutation associated with this disorder replaces the amino acid arginine with the amino acid lysine at protein position 1101 (written as Arg1101Lys or R1101K). It is unclear how this mutation causes FTD. This mutation likely alters the 3-dimensional shape of dynactin-1, which may impair its binding with the dynactin complex and microtubules. This impaired binding may slow the transport of materials needed for the proper function of axons and the efficient transmission of nerve impulses.

Chromosomal Location

Cytogenetic Location: 2p13.1, which is the short (p) arm of chromosome 2 at position 13.1

Molecular Location: base pairs 74,361,154 to 74,392,087 on chromosome 2 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- 150 kDa dynein-associated polypeptide
- DAP-150
- DP-150
- DYNA_HUMAN
- dynactin 1
- dynactin 1 (p150, glued homolog, Drosophila)

Additional Information & Resources

Educational Resources

- Molecular Cell Biology (fourth edition, 2000): Fast Axonal Transport Occurs along Microtubules
  https://www.ncbi.nlm.nih.gov/books/NBK21710/#A5453
- The Cell: A Molecular Approach (second edition, 2000): Identification of Microtubule Motor Proteins
  https://www.ncbi.nlm.nih.gov/books/NBK9833/#A1834
- Washington University, St. Louis Neuromuscular Disease Center
  http://neuromuscular.wustl.edu/synmot.html#vocaldyn

GeneReviews

- Amyotrophic Lateral Sclerosis Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1450
- Perry Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK47027

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28DCTN1%5BTIAB%5D%29+OR+%28dynactin+1%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- DYNACTIN 1
  http://omim.org/entry/601143
- FRONTOTEMPORAL DEMENTIA
  http://omim.org/entry/600274
- NEURONOPATHY, DISTAL HEREDITARY MOTOR, TYPE VIIB
  http://omim.org/entry/607641

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_DCTN1.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=DCTN1%5Bgene%5D
- HGNC Gene Family: Dynactin
  http://www.genenames.org/cgi-bin/genefamilies/set/943
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=2711
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/1639
- UniProt
  http://www.uniprot.org/uniprot/Q14203

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